REMARKS

Claims 1, 7-8, 12-13, and 65 are pending on the merits in this application for the Examiner's review and consideration upon entry of this paper. Claim 1 has been amended to more clearly recite the claimed invention. Support for the amendments can be found in the application as-filed. Claims 2-6, 9-11, and 14-64 have been cancelled without prejudice. Applicants reserve the right to file one or more divisional or continuation applications to any canceled subject matter. No new matter has been added by the amendments.

I. The Rejections Under 35 U.S.C. § 112, First Paragraph

Claims 1, 7-8, 12-13, and 65 are rejected on pages 2-4 of the office action under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the written description requirement.

Applicants respectfully submit that they have amended claim 1 thereby rendering the rejection to claim 1 and dependent claims 7-8, 12-13, and 65 moot. Accordingly, Applicants request that the rejection of claims 1, 7-8, 12-13, and 65 under 35 U.S.C. § 112, first paragraph, be withdrawn.

II. The Rejections Under 35 U.S.C. § 103

Claims 1, 9-13, and 65 are rejected on pages 4-8 of the Office Action under 35 U.S.C. §103(a) as allegedly obvious over U.S. Patent No. 5,962,437 to Kucera *et al.* ("Kucera") in view of Holmes et al., New England Journal of Medicine, 2003, Vol. 348, No. 20, pp. 1948-1951 ("Holmes").

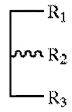
Applicants respectfully traverse the rejection for at least the following reasons.

The U.S. Supreme Court analyzed the test for obviousness in *KSR International Co. v. Teleflex Inc.*, 127 S. Ct. 1727 (2007). "There is no necessary inconsistency between the [teaching, suggestion, motivation] test and the Graham analysis. But a court errs where it transforms general principle into a rigid rule limiting the obviousness inquiry." *Id.* The Supreme Court's analysis in *KSR* relies on several assumptions about the prior art landscape. First, *KSR*

assumes a starting reference point or points in the art, prior to the time of invention, from which a skilled artisan might identify a problem and pursue potential solutions. Second, *KSR* presupposes that the record up to the time of invention would give some reasons, available within the knowledge of one of skill in the art, to make particular modifications to achieve the claimed compound. *See Takeda*, 492 F.3d at 1357. Third, the Supreme Court's analysis in *KSR* presumes that the record before the time of invention would supply some reasons for narrowing the prior art universe to a "finite number of identified, predictable solutions," *KSR* 127 S. Ct. at 1742. In *Ortho-McNeil Pharmaceutical, Inc. v. Mylan Laboratories, Inc.*, 520 F.3d 1358, 1364 (Fed. Cir. 2008), the Federal Circuit further explained that this "easily traversed, small and finite number of alternatives . . . might support an inference of obviousness." However, to the extent an art is unpredictable, as the chemical arts often are, *KSR's* focus on these "identified, predictable solutions" may present a difficult hurdle because potential solutions are less likely to be genuinely predictable. *Takeda Chemical Industries, LTD et al. v. Alphapharm PTY., Ltd.*, 492 F.3d 1350 (Fed. Cir. 2007).

The claims, as amended, encompass, *inter alia*, methods for treating a host infected with a togavirus or a coronavirus comprising administering an anti-viral effective amount of a compound or a pharmaceutically acceptable salt thereof, having a structure of Formula I:

(I)



wherein:

R_1 is —NHC(O)Y, where Y is C_1-C_{22} alkyl, C_2-C_{22} alkenyl, or C_2-C_{22} alkynyl;

R_2 is —OX, where X is C_1-C_{22} alkyl, C_2-C_{22} alkenyl, C_2-C_{22} alkynyl; and

R_3 is phosphocholine;

optionally with a pharmaceutically acceptable carrier or diluent.

According to the office action,

> Kucera *et al.* suggest and motivate the treatment of any type of virus type, especially membrane-containing or envelope containing viruses, wherein they teach that the compounds of Formula (I) disclosed therein attach to the cell membrane and thus are particularly effective against infections **caused by** membrane-containing or envelope-containing viruses. (col. 9, lines 42-45). Holmes *et al.* is provided as evidence that it was known in the art at the time of the invention that SARS corona virus contains a viral envelope (page 1949, right column and figure on page 1949).

(*See* Office Action at page 6, emphasis in original).

The office action admits:

> The cited reference differs from the instant claims in the length of the alkyl chains at R_1 and R_2 in the compounds of Formula (I). For example, the elected compound of Formula (I) has a C_{22} alkyl chain at R_1 and R_2, whereas the reference limits these substituents to C_6 to C_{18} alkyl and C_6 to C_{14} alkyl, respectively. Kucera also differs from the claims in that the reference does not disclose the treatment of a corona virus (*e.g.,* SARS-CoV).

(*Id.*).

The office action further states:

> Kucera, in contrast to Applicant's characterization, does provide a working mechanism with regard to the used of lipods in treating virus infections, especially membrane-containing or envelope-containing viruses, wherein they teach that compounds of Formula (I) disclosed therein attach to the cell membrane and thus are particularly effective against infections **caused by** membrane-containing or envelope-containing viruses. (col. 9, lines 42-45).

(*Id.* at page 8, emphasis in original).

Thus, the essence of the Examiner's rejection can be summarized as even though Kucera does not disclose the claimed methods of treatment recited by the claims, the fact that Kucera discloses membrane-containing or envelope-containing viruses and the claimed disorders are envelope-containing viruses as evidenced by Holmes, the claims would nonetheless be obvious. The Examiner's allegations are inconsistent with the current law on obviousness. Indeed, the

assertion in the office action that "Kucera *et al.* suggest and motivate the treatment of any type of virus type, especially membrane-containing or envelope containing viruses" is not proper. (Applicants' emphasis). As the Examiner is aware, the record before the time of invention must supply some reasons for narrowing the prior art universe to a "finite number of identified, predictable solutions. *See KSR* 127 S. Ct. at 1742. The Examiner has provided no motivation to modify the disorders disclosed in Kucera to obtain the claimed methods of treatment. The fact that the viruses in Kucera and the claimed viruses both have a viral envelope would provide no motivation (with or without Holmes) to modify the teaching of the reference to obtain the claimed invention. Indeed, many viruses (*e.g.,* influenza and many animal viruses) have viral envelopes covering their protein capsids. The envelopes are typically derived from portions of the host cell membranes (phospholipids and proteins), but include some viral glycoproteins. Functionally, viral envelopes are used to help viruses enter host cells. Glycoproteins on the surface of the envelope serve to identify and bind to receptor sites on the host's membrane. The viral envelope then fuses with the host's membrane, allowing the capsid and viral genome to enter and infect the host. Therefore, the fact that two viruses have a viral envelope in common would not suggest to one of ordinary skill in the art that the virus could be treated in the same way. For example, it would not be obvious to one of ordinary skill in the art to treat murine leukemia virus (which contains a viral envelope glycoprotein) the same way one would consider treating influenza virus (which also contains a viral envelope) merely because both viruses contain a viral envelope. Moreover, it is generally accepted that the lipids in virus envelopes are derived from the host cell. This is shown by the facts that: (i) viruses rarely have lipids not found in host cells, (ii) when viruses are grown in different host cells, they show differences in their lipid patterns, and (iii) radioactively labeled cellular lipids are incorporated into virions. The different classes of lipids present in viral envelopes include (a) Phospolipids, (b) Cholesterol, (c) Fatty acids, and (d) Glycolipids.

Even assuming *arguendo* that the fact that the disorders disclosed in Kucera are membrane-containing or envelope containing viruses and the claimed corona virus is an envelope containing virus, this does not rise to the level of a motivation to modify the reference. Indeed,

this "easily traversed, small and finite number of alternatives . . . might support an inference of obviousness." *Ortho-McNeil Pharmaceutical, Inc. v. Mylan Laboratories, Inc.*, 520 F.3d 1358, 1364 (Fed. Cir. 2008). However, to the extent an art is unpredictable, as the chemical arts often are, *KSR's* focus on these "identified, predictable solutions" may present a difficult hurdle because potential solutions are less likely to be genuinely predictable. *Takeda Chemical Industries, LTD et al. v. Alphapharm PTY., Ltd.*, 492 F.3d 1350 (Fed. Cir. 2007).

Applicants respectfully submit that the combination of Kucera and Holmes does not provide the legally required motivation to modify the teachings of the references to obtain the claimed invention. Indeed, the combination of references neither teaches nor suggests the treatment of a *togavirus* or a *coronavirus* using the compounds of Formula (I) as recited by the pending claims.

For at least the above reasons, Kucera and/or Holmes alone or in combination do not render claims 1, 7-9, 12-13 and 65 obvious. Applicants respectfully submit that the rejections of claims 1, 7-9, 12-13 and 65 under 35 U.S.C. § 103 (a) should be reconsidered and withdrawn.

III. Conclusion

It is respectfully submitted that the rejections to the claims have been overcome. Should the Examiner disagree, Applicants respectfully request a telephonic or in-person interview with the undersigned attorney to discuss any remaining issues and to expedite the eventual allowance of the claims.

Except for issues payable under 37 C.F.R. § 1.18, the Commissioner is hereby authorized by this paper to charge any additional fees during the entire pendency of this application including fees due under 37 C.F.R. 1.16 and 1.17 which may be required, including any required extension of time fees, or credit any overpayment to Deposit Account 50-0310.

Respectfully submitted,
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